There are current indications for pericardial biopsy: (1) Chronic or recurrent pericarditis of uncertain etiology; (2) unexplained hemopericardium, and (3) possibly constrictive or adhesive pericarditis.[17]

In the present case the early diagnosis by pericardial biopsy was of no ultimate benefit to the patient, and the chemotherapy was of questionable value.

Summary

A case of primary malignant mesothelioma of the pericardium is reported. The case would appear to support the rationale of early open pericardial biopsy in refractory pericarditis where diagnosis cannot be established by other means.

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Eye Damage in Newborns From Use of Strong Silver Nitrate Solutions

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AFTER MORE THAN a decade of controversy, silver nitrate solution is still the most widely used prophylactic agent for preventing gonorrheal ophthalmitis in the newborn. In March of 1966 the California State Department of Public Health noted[7] that nine cases of gonorrheal ophthalmia had been reported in three and a half months, a reminder that the disease is not extinct. In 1 per cent concentration, silver nitrate is probably the safest and most efficacious agent for the Crede procedure.[1] However, ocular damage resulting from misapplication of other silver nitrate concentrations has been reported by Dieckmann,[3] Lehrfeld[5] and Davidson and coworkers.[2] Two cases of permanent and severe eye injury following the accidental substitution of ammoniacal silver nitrate solution (25 to 35 per cent) for the 1 per cent strength are reported herein.

These cases may be unusually significant in the context of a recent decision which could in-

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crease a potential hazard for every infant delivered in the State of California. In September 1965, the State Department of Public Health informed health officers and hospital administrators throughout California that the Department would no longer supply silver nitrate solution in wax ampoules "to persons engaged in the practice of obstetrics or assisting at childbirth." This decision appears to be based on a desire of the Department of Public Health to eliminate a function which, although not very costly to the state, could be left to the using medical facilities.

Continuing centralized procurement of ophthalmic silver nitrate, although no longer required by law, might reduce a hazard which few California physicians suspect. When the author saw the first of two infants with ocular damage from too strong a solution of ammoniacal silver nitrate, it seemed unlikely that he ever would see another. That he did, gives both of them extraordinary significance.

CASE 1.—In August 1951 a term male infant, weighing 7 pounds 7 ounces, was delivered following an uneventful pregnancy. The infant appeared normal. About seven hours later he was noted by nursery attendants to have severe redness and swelling of both eyelids and a purulent ocular discharge. A pediatrician examined the infant and recognized that the eye inflammation was too severe to attribute to any common infection so soon after a normal birth. Saline and boric acid irrigations and compresses were used liberally. An ophthalmologist was consulted, and topical treatment of the inflamed conjunctivae was given with cortisone ointment and antibiotics.

Dark brown stains on one eyelid and the cheek suggested chemical injury. Investigation revealed that the only silver nitrate present in the delivery room was packaged in brown glass ampoules which bore the label "silver nitrate solution, ammoniacal." This is a dental caustic, commonly dispensed in 25 to 35 per cent strengths. *But the strength is not stated on the label.*

Fortunately the discovery that this potent solution had been erroneously substituted for the traditional, single-dose, wax ampoules of 1 per cent silver nitrate was made before it could be used on other infants. At least four medically trained persons had had opportunity to detect this substitution but had not recognized the error. Investigation determined that the error originated with the hospital pharmacy.

The infant was observed and treated by the ophthalmologist for a prolonged period. The initial injury included corneal opacity of the left eye and severe inflammation of both conjunctivae. Partial scarring of the left cornea persisted and there was decided reduction of visual acuity of that eye.

CASE 2.—A term male infant, weighing 7 pounds 3½ ounces, was delivered at home in October 1960, following precipitous labor. The mother and infant were examined in the home by a physician, then were taken by ambulance to a nearby dispensary. No abnormalities were found in either patient and the unattended delivery had been without apparent complications. A physician instilled silver nitrate into both of the infant's eyes. The baby responded with cries of pain and the physician "immediately washed the eyes with a constant sterile saline flush for five minutes to both eyes."

Five hours after delivery, the infant was noted to have pronounced swelling of both eyelids and a seropurulent conjunctival discharge. Irrigations with saline solution were again used and polymyxin-neomycin-bacitracin ophthalmic ointment applied. The infant was transferred to the "suspect nursery" of a nearby hospital. Bacterial conjunctivitis was suspected because of the unsterile delivery, and penicillin and streptomycin were administered parenterally.

The presumed infectious conjunctivitis did not improve with topical therapy. The next day cultures of pus from the eyes revealed a mixed infection of Aerobacter aerogenes, diphtheroids and coagulase-negative staphylococci. The infant showed no signs of illness except chemosis and purulent ocular discharge. At first, adequate inspection of the corneas was impossible. Three days later, a consulting ophthalmologist described the infant as having decided mucopurulent conjunctivitis, keratitis and corneal opacity of the left eye. The right eye was felt to show "slight involvement."

The true cause of the conjunctivitis was not recognized until ten days after delivery. After antiinfectious therapy failed, hospital physicians asked the dispensary personnel to review the events subsequent to delivery. Only then was it recognized that ammoniacal silver nitrate (25 to 35 per cent) had been substituted in the emergency obstetrical kit for the wax ampoules of 1 per cent silver nitrate solution. A pharmacy had issued the dental preparation of silver nitrate when unable to supply the wax ampoules.

After six weeks, the infant was transferred to

Letterman General Hospital for further care. Diagnoses listed on the record cover sheet at that time included: "(1) Burn, chemical, left eye. (2) Opacity, cornea, left. (3) Ulcer, cornea, left. (4) Blepharitis, left. (5) Conjunctivitis, left. (6) Symblepharon, left. (7) Entropion, cicatricial, left."

On the advice of several ophthalmologists, definitive surgical correction of the conjunctival and corneal lesions of the left eye was not attempted until the child reached age two years. In 1963, 1964 and 1965, nine separate plastic surgical procedures were carried out in an attempt to restore function and improve the appearance of the left eye. At the most recent examination, the eye had no useful vision.

Discussion

Silver nitrate solution in 1 per cent concentration is well established as an effective agent in prophylaxis of ophthalmia neonatorum. There are no reports of lasting eye damage from this strength of silver nitrate. Mathieu[6] reported a comparative study in which 2 per cent silver nitrate solution and oxytetracycline were used for gonorrheal prophylaxis and observed no lasting effects of either drug at a follow-up examination six weeks after delivery. Thus, it appears that at least twice the usual concentration of silver nitrate is safely tolerated by infant eyes. Reports of corneal and conjunctival damage due to silver nitrate solution have, without exception, followed the use of this chemical in 5 per cent or greater concentrations.

Harrison[4] described the action of silver nitrate as follows: "When a 1 per cent solution of silver nitrate is applied to mucous membrane of the eye, the protein in the tissue is coagulated or precipitated by the chlorides present in the tissues. This produces alterations in the permeability of the superficial cells so that there is decreased secretion. The silver chloride produced is an antiseptic and since it is precipitated in the superficial layers, its action is not transitory, and its effects may last several days."

This description of the pharmaceutical action of silver nitrate on the ocular mucous membrane might also imply that a beneficial decrease in permeability to bacterial organisms results from the Crede procedure. The successful use of 1 per cent silver nitrate in the eyes of millions of babies attests the safety of the superficial amount of protein coagulation. Persistence of antibacterial activity or favorable alteration of the mucous membrane epithelium has not been claimed for one-dose antibiotic ointments or solutions.

The two cases reported here of eye injury from ammoniacal silver nitrate may indicate a particular hazard for babies born in medical installations of the U.S. Armed Forces. Many military hospitals have under one roof both dental and medical facilities which share the same pharmacy. However, it seems reasonable to assume many other circumstances that might lead to substitution of stronger silver nitrate solutions could exist in any hospital. When a pharmacy is unable to supply the obstetrical service with 1 per cent silver nitrate in wax ampoules, a possibility of disastrous substitution exists. The larger the hospital, often the more overburdened is the pharmacy. It is not uncommon for persons other than licensed pharmacists to be given the actual responsibility of taking medications from a stock-room shelf and delivering them to a ward or clinic. Although in the cases here reported, several professional personnel had an opportunity to detect this hazard before it could harm an infant, they did not recognize the error.

Familiarity with the traditional wax ampoule of 1 per cent silver nitrate is not sufficiently widespread among medical personnel. When interns who had just completed their obstetrical rotation at this hospital were questioned recently, it was found that some had never given the Crede prophylaxis during either their internship or clinical clerkship. They did not know that only the wax ampoules should be used.

Ironically, although single dose wax ampoules cannot be permanently labeled individually, practically no other medication in popular use is similarly packaged. Proper identification of these ampoules must depend upon the container in which they are issued rather than the ampoules themselves. Thus, the safety paradox which requires that persons caring for newborn infants reject for ophthalmic use any silver nitrate ampoule which bears the name of the drug.

Subject to the most stringent requirements of quality control and labeling, manufacturers engaged in interstate commerce are the logical source of mass-produced items of single-dose size. They sell ophthalmic silver nitrate solution, 1 per cent, in wax ampoules, to the Federal Government for $1.80 per package of 24 units. Other users of

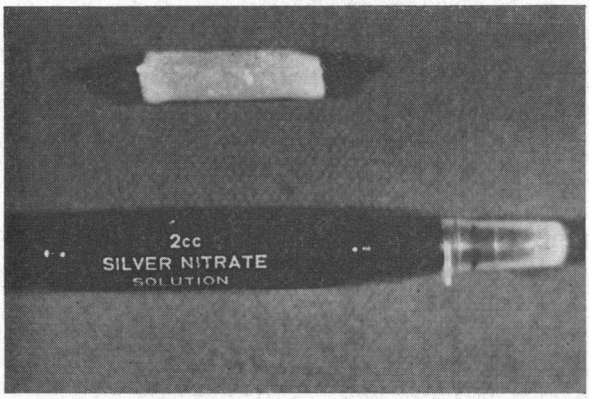

Figure 1.—Ampoules of 1 per cent silver nitrate (wax) and 35 per cent dental preparation (amber glass), showing total lack of similarity of appearance.

large quantities should be able to obtain similar low prices.

Centralized procurement, on a statewide scale, of silver nitrate solution has probably spared many California babies ocular damage. Should not familiarity with one packaging of the safe solution be insured by every means possible? Figure 1 shows containers that it would seem could not have been confused, but were. If the state does not continue this protection, is there not another organization with professional concern sufficient to assume this responsibility and modest expense? Direct dispensing from a central source to obstetrical services, by-passing the possibility of pharmacy error, might be a worthwhile added safety precaution.

Summary

Two cases of permanent ocular damage due to accidental application of ammoniacal silver nitrate (25 to 35 per cent) in the newborn period are reported. The accidents illustrate a hazard deserving timely consideration, associated with the California State Department of Public Health's discontinuance of its practice of supplying silver nitrate solution in wax ampoules for lavage of newborn babies' eyes.

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Haemophilus Influenza Type b Orbital Cellulitis

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IN CHILDREN, orbital cellulitis, an inflammation of the cellular tissues of the orbit, is usually an extension of bacterial infection of the paranasal sinuses.[5] *Streptococci*,[4] *Staphylococci* and *Escherichia coli*[6] have been implicated etiologically. Reports of only three cases of orbital cellulitis due to *Haemophilus influenzae* type b have appeared in the English language literature.[1,3]

During November and December 1965 three children with orbital cellulitis were admitted to the Childrens Hospital of Los Angeles. In each instance *H. influenzae* type b grew on culture of the blood. The purpose of this paper is to report these three cases and to compare them with the cases of other patients with orbital cellulitis admitted to the Childrens Hospital of Los Angeles during the five-year period 1960-1965.

Reports of Cases

CASE 1.—An eight-month-old Mexican-American boy in whom the diagnosis of Sturge-Weber syndrome had been made was admitted to hospital four hours after swelling and tenderness developed in the right orbital area.

On admission the temperature was 40°C (104°F), the pulse rate 144 per minute, respirations 30 per minute and the blood pressure (Flush method) 100 mm of mercury. The right orbital area was massively swollen and purulent conjunctivitis was present. A hemangioma involved the right side of the face and neck. Except for generalized hypotonia no other abnormalities were noted on physical examination.

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